Enabling technologies for cyclodextrins complexation, funtionalization and material grafting

ENABLING TECHNOLOGIES FOR CYCLODEXTRINS COMPLEXATION, FUNCTIONALIZATION AND MATERIAL GRAFTING

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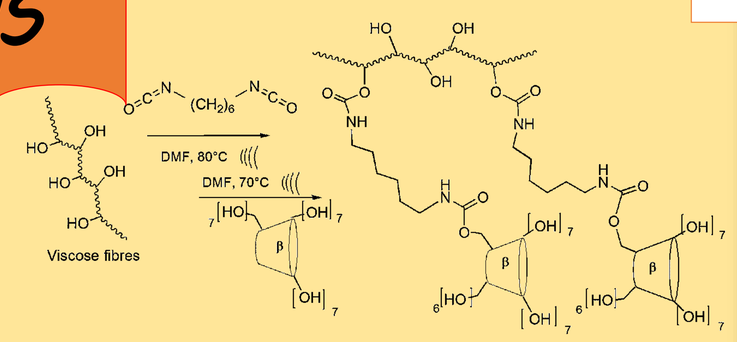
Synthetic chemists are increasingly paying attention to combinations of enabling technologies with an eye to achieving the double goal of obtaining high efficiency and meeting the green criteria of energy savings and the absence of dangerous or harsh reagents. Microwave (MW)[1,2] power ultrasound (US)[3], hydrodynamic cavitation[4] ball milling[5] and hybrid flow-reactors[6] are a valid and versatile alternative for process intensification in organic synthesis.[7] Herein we present few applications of these technologies for the treatment of cyclodextrins (CDs) to obtain interesting compounds in very different fields. β-CDs are natural cyclic oligosaccharides, formed by (R-1,4)-linked R-D-glucopyranose units, and possess a basket-shaped topology with an inner cavity which exhibits a relatively non-polar behavior. Thanks to these features β-CDs are able to form reversible, non-covalent inclusion complexes with guest molecules (G) that dimensionally fit inside the cavity and are less polar than water.

US



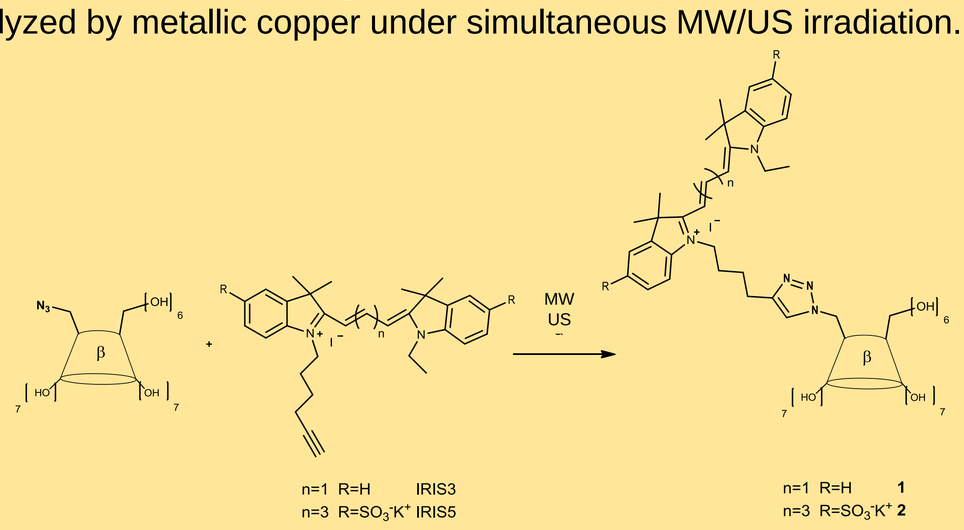
Immersion horn 20.1 kHz

Synthesis of β-CD-grafted viscose has been developed by means of a two step US-assisted reaction: first with hexamethylene diisocyanate (HDI), as cross-linkers, and then with native β-CD. The grafted fabric has been characterized by ATR-FTIR, CP-MAS spectra and by an phenolphthalein empiric colorimetric method. By the spectroscopic characterization of the products, this US-assisted grafting is fast and repeatable. We have formulated a suitable cosmetic preparation to charge the CD-grafted textile. Permeation and accumulation studies on membranes and porcine ear skin showed the advantages of this cosmeto-textile for its potential application in the treatment of venous insufficiency in legs. The low production costs, optimal application compliance and easy fabric recharging lay the foundations for future industrial production.[8]

MW-US

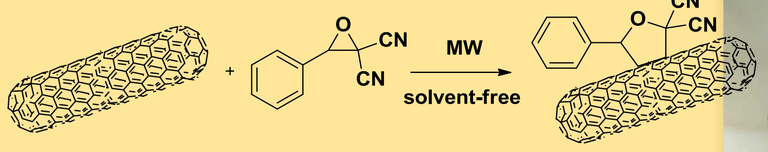
MW/US combined multimode oven

β-CDs are able to form reversible, non-covalent inclusion complexes with guest molecules with apolar behaviour. Various kinds of dye moiety appended CD derivatives were proposed to be used like "turn on" or "turn off" fluorescent chemical sensors, in which fluorescence intensity is enhanced or decreased by complexation with guest molecules. Due the well-known limitation of the CD derivatization reactions, MW and US irradiation were exploited for the mono-functionalization of the N_3- β-CDs catalyzed by metallic copper (Cu). The use of US favors mechanical depassivation, enhances both mass transfer and electron transfer from the metal to the organic acceptor and avoid the formation of β-CDs complexes with copper ions. Two new cyanine- β-CDs derivatives have been synthesized through azide-alkyne cycloadditions efficiently catalyzed by metallic copper under simultaneous MW/US irradiation.

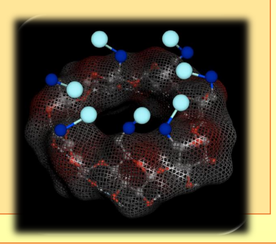


MW-SRC

SynthWave



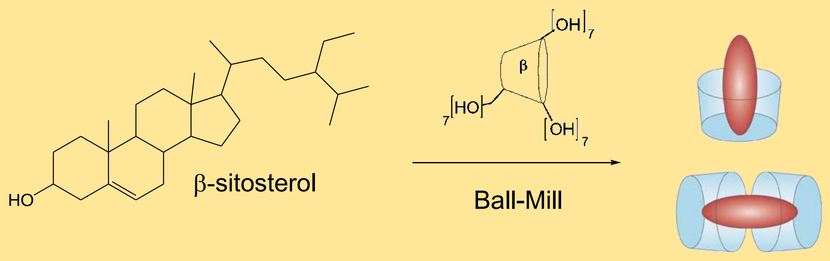
We set up an efficient solvent-free MW-assisted protocol that afford highly functionalized SWCNTs via 1,3-dipolar cycloaddition of carbonyl ylides. The reactive functional groups on these highly water-dispersible SWCNTs derivatives enable further functionalization paving the road for several potential applications. The SRC instrument allow to perform the reaction under 20 bar of N_2 avoiding air oxidation and to obtain a homogenous and regular heating of the solid sample since the reaction vessel is immersed in water as adsorbing medium and the stirring is very efficient. Further functionalization with CD are still in progress to obtain systems useful for biomedical applications.[9]
The SRC device has also been exploit to optimise non conventional reliable procedures for the synthesis of per-substituted cyclodextrins bearing amino, urea and thiourea groups on the primary face. To obtain more hydrophilic compounds volatile amines such as allylamine and butylamine were selected reacted in a MW reactor SynthWAVE. This system is a closed-vessel system allowing reactions to be performed under significant pressures and temps.[10]



BALL-MILL

Planetary ball mill PM100

β-CD, which is widely used to increase the stability, solubility, and bioavailability of guests, can form host–guest inclusion complexes with a wide variety of organic molecules.
Ball-milling technique was employed for the formation of CD inclusion with steroid molecules of synthetic and pharmaceutical interest without the use of any solvent. In only 40 minutes at 200 rpm it has been possible to obtain a complexation efficiency around 90% with a CD/steroid structure molecular ratio of 2:1. The method has been set up with β-sitosterol as target compound and applied also to cholesterol and cholic acid with successful results.



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